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EXAMINER
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ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,416	RIEPING ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/27/04, 1/26/05, 8/3/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28 and 30-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28,30-34 and 39-41* is/are rejected.

7)☒ Claim(s) *35-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/26/2005 has been entered.

[2] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[3] Claims 23-28 and 30-41 are pending in the application.

[4] Applicants' amendments to the claims, filed on 1/26/2005 and 8/3/2005, are acknowledged. The claim listing filed on 1/26/2005 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) set forth in the Office communication mailed on 4/21/2005. The claim listing filed on 8/3/2005 replaces all prior versions and listings of the claims.

[5] Applicants' arguments filed on 12/27/2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objection

[7] Claims 40 and 41 are objected to as not ending with a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

[8] Claim(s) 23-28, 30-34, and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 23 (claim(s) 24-28, 30-34, 39, and 41 dependent therefrom) and 40 are indefinite in the recitation of "insertional mutagenesis due to homologous recombination" as it is unclear as to whether the inactivation of the gene is due to insertional mutagenesis of the poxB gene, or whether the inactivation is due to insertional mutagenesis to another unspecified gene, *e.g.,* insertional mutagenesis to a gene encoding a transcription factor that controls expression of the poxB gene. In the interest of advancing prosecution, the examiner has interpreted the term as meaning insertional mutagenesis due to homologous recombination in the poxB gene. It is suggested that applicants clarify the meaning of the claim.

[b] Claim 23 (claim(s) 24-28, 30-34, and 39-41 dependent therefrom) is confusing in the recitation of "eliminated poxB gene," which suggests that the gene encoding PoxB is removed from the microorganism. However, the claim indicates that the gene can remain, albeit in a mutated form. Thus, according to the claim, the poxB gene may not

be eliminated, only inactivated. It is suggested that applicants clarify the meaning of the claim.

[c] Claim 34 recites the limitation "the *E. coli* yjfA or *E. coli* yftP." There is insufficient antecedent basis for this limitation in the claim.

[d] In view of the recitation of "homologous recombination, and," it appears that additional text was meant to be included in claim 40. As such, claim 40 appears to be incomplete. It is suggested that applicants complete the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[9] Claims 23-28, 30-34, and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 23 (claim(s) 24-28, 33, and 39-41 dependent therefrom) is drawn to a process for producing an L-amino acid by culturing a genus of modified microorganisms of the *Enterobacteriaceae* family comprising an eliminated poxB gene. Claim 30 is drawn to the method of claim 23 wherein the genus of modified microorganisms further comprises at least one overexpressed gene product encoded by a gene selected from at least one gene encoded by thrABC operon, pyc, pps, ppc, pntA and pntB, rhtB, mqo, rhtC, *C. glutamicum* thrE, and gdhA. Claims 31 and 34 are drawn to the method of claim 23 wherein the genus of modified microorganisms further comprises at least one gene

whose expression is reduced or eliminated selected from tdh, mdh, pckA, *E. coli* yjfA or *E. coli* ytfP.

The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "In claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the genus of recited modified microorganisms, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the nucleic acid species within the genus from other nucleic acids such that one can visualize or recognize the identity of the members of the genus.

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant,

identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Regarding claim 23, the specification discloses only a single species of the genus of recited modified microorganisms of the *Enterobacteriaceae* family comprising an eliminated poxB gene, *i.e., Escherichia coli* comprising an inactivated poxB gene, wherein the poxB gene has the nucleotide sequence of SEQ ID NO:1. Although it is noted that the specification discloses three species of the genus, MG442poxB (p. 15), TOC21RpoxB (p. 21), and B-1288poxB (p. 23), all of these species fall within the scope of the broader species described above. Other than this single disclosed species, the specification fails to disclose any other additional representative species of the genus of modified microorganisms of the *Enterobacteriaceae* family comprising an eliminated poxB gene. Regarding claims 30-31 and 34, it is noted that modified microorganism has *any* modification that results in overexpression of the recited gene product or *any* modification that results in reduction or elimination of the recited gene. Also, according to applicants, the specification discloses a species of each genus of recited genes (pp. 9-10). However, while MPEP § 2163 acknowledges that in certain situations “one

species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus".

Thus, given the lack of description of a representative number of genes, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

RESPONSE TO ARGUMENT: Applicants argue that in view of the amendment to the claims, a skilled artisan would recognize that the specification describes the claimed invention. However, even in view of the amendment to the claims, this is not found persuasive at least for the reasons stated above.

[10] Claims 23-28, 30-34, and 39-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of claim 23 using an *E. coli* having an inactivated poxB gene of SEQ ID NO:1, optionally wherein the *E. coli* further comprises an expression vector or vectors encoding thrA, thrB, thrC, pyc, pps, ppc, pntA and pntB, rhtB, mqo, rhtC, *C. glutamicum* thrE, and gdhA as disclosed in the reference(s) cited at p. 9 of the specification and/or having an inactivated gene as disclosed in the reference(s) at p. 10 of the specification, does not reasonably provide enablement for the method of claim 23 using all modified microorganisms as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claim 23 encompasses the use of any "modified microorganism of the *Enterobacteriaceae* family" that has any "eliminated poxB gene which encodes a pyruvate oxidase." Claim 30 encompasses the "modified microorganism of the *Enterobacteriaceae* family" of claim 23 further comprising an "overexpressed gene product," wherein the gene and its product have any structure

including mutants and variants, and wherein overexpression is achieved by any method. Claims 31 and 34 encompass the "modified microorganism of the *Enterobacteriaceae* family" of claim 23 further comprising an "at least one gene whose expression is reduced or eliminated," wherein the gene has any structure and wherein decreased expression is achieved by any method. The enablement provided by the specification is not commensurate in scope with the claims with regard to the broad scope of microorganisms of the *Enterobacteriaceae* family that have an eliminated poxB gene, modifications to microorganisms of the *Enterobacteriaceae* family that result in increased expression of a "gene product" or decreased expression of a gene, the scope of overexpressed gene products, and the scope of inactivated genes.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: According to the specification, at the time of the invention, the prior art disclosed an *E. coli* poxB gene (see p. 6, top). However, at the time of the invention, it was highly unpredictable as to whether this *E. coli* poxB gene shared sufficient structural identity to poxB genes of all other microorganisms of the *Enterobacteriaceae* family such that one of skill in the art could isolate all of the poxB genes of all microorganisms of the *Enterobacteriaceae* family in order to mutationally inactivate the poxB gene of the corresponding microorganism. Similar reasoning applies to claims 31 and 34. Also, regarding claims 30-31 and 34, it is highly unpredictable as to those modifications as broadly encompassed by the claims that can be made to any microorganisms of the *Enterobacteriaceae* family that result in a microorganism having the desired activity/utility.

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only a single working example of the recited poxB gene, *i.e.*,SEQ ID NO:1. The specification discloses only two working examples of the modified microorganisms as encompassed by claim 30 (see examples 5-6 at pp. 17-20 of the specification). Other than these working examples, the specification fails to provide the guidance that is necessary in making the full scope of recited modified microorganisms of the *Enterobacteriaceae* family. The specification fails to disclose even a single working example of the modified microorganisms of the *Enterobacteriaceae* family as encompassed by claims 31 and 34.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating homologous genes in related organisms were known in the art at the time of the invention, it was not routine in the art to isolate all poxB genes in all microorganisms of the *Enterobacteriaceae* family and to modify the corresponding microorganism to inactivate its poxB gene. Further, it was not routine to increase expression of a desired gene by any method and it was not routine to inactivate a desired gene by any method in any modified microorganism of the *Enterobacteriaceae* family.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make

and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: Applicants argue that in view of the amendment to the claims, a skilled artisan would recognize that the specification enables the full scope of the claimed invention. However, even in view of the amendment to the claims, this is not found persuasive at least for the reasons stated above.

Claim Rejections - Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[11] The following are provisional rejections:

[a] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/483,983 (the '983 application).

[b] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 13 of co-pending US non-provisional application 10/794,417 (the '417 application).

[c] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/483,416 (the '416 application).

[d] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/784,914 (the '914 application).

[e] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/784,902 (the '902 application).

[f] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 27 of co-pending US non-provisional application 11/017,120 (the '120 application).

[g] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/483,413 (the '413 application).

[h] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/481,634 (the '634 application).

[i] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/481,745 (the '745 application).

[j] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 18 of co-pending US non-provisional application 10/937,598 (the '598 application).

[k] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 18 of co-pending US non-provisional application 10/937,554 (the '554 application).

[l] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/491,893 (the '893 application).

[m] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/481,746 (the '746 application).

[n] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/484,198 (the '198 application).

[o] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 14 of co-pending US non-provisional application 10/619,309 (the '309 application).

[p] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/483,417 (the '417 application).

[q] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/481,823 (the '823 application).

[r] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/481,743 (the '743 application).

[s] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 14 of co-pending US non-provisional application 10/817,431 (the '431 application).

[t] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of co-pending US non-provisional application 10/812,315 (the '315 application).

[u] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of co-pending US non-provisional application 10/733,776 (the '776 application).

[v] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of co-pending US non-provisional application 10/416,364 (the '364 application).

[w] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-14 of co-pending US non-provisional application 10/114,048 (the '048 application).

[x] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-14 of co-pending US non-provisional application 10/114,043 (the '043 application).

[y] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-14 of co-pending US non-provisional application 10/114,073 (the '073 application).

[z] Claims 23, 31, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of co-pending US non-provisional application 10/186,999 (the '999 application).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from

each other because the claims of the '983, '417, '416, '914, '902, '102, '413, '634, '745, '598, '554, '893, '746, '198, '309, '417, '823, '743, '431, '315, '776, '364, '048, '043, '073, and '999 applications anticipate claims 23, 31, and 34 herein or the specifications of the applications support an embodiment that would anticipate claims 23, 31, and 34 herein. Claims 23, 31, and 34 of the instant application cannot be considered to be patentably distinct over the claims of the '983, '417, '416, '914, '902, '102, '413, '634, '745, '598, '554, '893, '746, '198, '309, '417, '823, '743, '431, '315, '776, '364, '048, '043, '073, and '999 applications as noted above when there is a specifically recited embodiment that falls within the scope of claims 23, 31, and 34 herein. Alternatively, claims 23, 31, and 34 cannot be considered to be patentably distinct when there is a specifically disclosed embodiment in the applications that supports the claims and falls within the scope of claims 23, 31, and 34 herein because it would have been obvious to one of ordinary skill in the art to modify the claimed methods by specifically using an Escherichia host with inactivated poxB and pckA, yjfA, or ytfP genes. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

[12] The examiner has made an earnest attempt to identify those patents and/or co-pending applications for purposes of rejecting or provisionally rejecting the claims for double patenting. However, it is noted that numerous co-pending applications have been filed and/or continue to be filed, and/or patents have issued disclosing subject matter that is related to the instant application. In the interest of compact prosecution,

the examiner requests that: 1) applicants identify any patent(s) and/or co-pending application(s) that claim(s) subject matter that may necessitate a double patenting rejection, an obviousness-type double patenting rejection, a provisional double patenting rejection, or a provisional obviousness-type double patenting rejection; 2) identify the claims of the patents and/or co-pending applications that claim identical or similar subject matter; 3) identify the corresponding claims of the instant application, and 4) take the appropriate action, *e.g.*, cancel claims to preempt a statutory double patenting rejection and/or file a terminal disclaimer to preempt an obvious-type double patenting rejection or provisional rejection. Applicants' cooperation in following steps 1) to 4) above is appreciated as this will allow the examiner to focus on more substantive issues in the examination of the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[13] Claim(s) 23, 25-28, 33, and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang et al. (*J Bacteriol* 154:756-762). The claims are drawn to a

method for producing an L-amino acid by fermenting a microorganism of the *Enterobacteriaceae* family and isolating the L-amino acid.

Chang et al. teaches an *E. coli* mutant with an inactivated poxB gene, wherein the gene is inactivated by insertion of a transposon into the poxB gene (see, *e.g.*, p. 758, Table 2 and p. 759, right column). Chang et al. teaches culturing of the *E. coli* mutant and recovering a cell-free extract from the crude cellular lysate (see, *e.g.*, p. 756, right column). This anticipates claims 23, 25-28, 33, and 40 as written.

For purposes of clarifying the record, the following examiner's comments are provided. While Chang et al. does not teach isolation of *only* an L-amino acid from the cultured cells, Chang et al. does teach isolation of a cell-free extract from a crude cellular preparation, which would comprise L-amino acids, including L-threonine, L-valine, and L-lysine, which are endogenously produced by *E. coli*. In accordance with MPEP 2111, it is the examiner's position that isolation of the cell-free extract from the crude cellular preparation is considered to be "isolating the L-amino acid" from the cellular debris. In this case, there is no definition of the term "isolating" with respect to an L-amino acid in the specification and there is no limitation in the claim that requires the L-amino acid to be free of additional elements of a cell-free extract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole

> would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[14] Claim(s) 23-28, 30-34, and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riepling et al. (US Patent 6,916,637) in view of Dusch et al. (US Patent Application Publication 2005/0196848), Chang et al. (*supra*), and Grabau et al. (*Nucleic Acids Res* 14:5449-5460; cited in the IDS filed on 9/3/2002). The claims are drawn to a method for producing an L-amino acid by fermenting a microorganism of the *Enterobacteriaceae* family and isolating the L-amino acid.

Riepling et al. teaches that *E. coli* is used in the fermentative production of L-amino acids (column 1). Riepling et al. teaches the construction of *E. coli* having inactivated pckA and/or yftP-yjfA genes, optionally overexpressing gdhA or rhtC genes (columns 4-5 and Examples 1-3 and 11-13) and further teaches specific methods for producing L-threonine, L-lysine, and L-valine using said *E. coli* (Examples 4-10 and 14-15). The *E. coli* of Riepling et al. used in the production of L-amino acids do not have an inactivated poxB gene. The teachings of Riepling et al. were first disclosed in provisional application 60/237,610, filed on 10/4/2000.

Dusch et al. teaches a method for L-lysine production using a *C. glutamicum* having an inactivated *poxB* gene, wherein inactivation of the poxB gene results in an approximate 50% increase in the production of L-lysine (p. 6, Example 5).

Chang et al. discloses the teachings as described above. Notably, the results of Chang et al. indicate that inactivation of the *poxB* gene in *E. coli* is not lethal (see particularly p. 758, left column, middle).

Grabau et al. teaches the nucleic acid sequence of an *E. coli poxB* gene (see particularly p. 5452).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Riepling et al., Dusch et al., Chang et al., and Grabau et al. to inactivate the *E. coli poxB* gene in the *E. coli* strains of Riepling et al., culture the resulting *E. coli,* isolate the resulting medium and cell extract, and determine the levels of resulting L-amino acids, particularly L-threonine, L-lysine, and L-valine. One would have been motivated to do this because attenuation of poxB in *C. glutamicum* resulted in an increased production of an L-amino acid and, like *C. glutamicum, E. coli* is used to produce L-amino acids, and "attempts are constantly being made to improve" L-amino acid production as acknowledged by Reipling et al. (column 1, lines 19-41). One would have a reasonable expectation of success for inactivating the *E. coli poxB* gene in the *E. coli* strains of Riepling et al., culturing the resulting *E. coli,* isolating the resulting medium and cell extract, and determining the levels of resulting L-amino acids because of the results of Dusch et al., Chang et al., Riepling et al. and Grabau et al., particularly in view of the teaching of Chang et al. that an *E. coli* having an inactivated poxB gene is viable. Therefore, claims 23-28, 30-34, and 39-41, drawn to the method described above, would have been obvious to one of ordinary skill in the art.

Citation of Relevant References

[15] The reference(s) made of record and not relied upon is/are considered pertinent to applicant's disclosure. Vemuri et al. (*Biotechnol Bioeng* 90:64-76) teaches an

analysis of the effects of simultaneously deleting the poxB gene and overexpressing the pyc gene in *E. coli.* The reference, being published in 2005, is not available as prior art.

Conclusion

[16] Status of the claims:

Claims 23-28 and 30-41 are pending.

Claims 23-28, 30-34, and 39-41 are rejected.

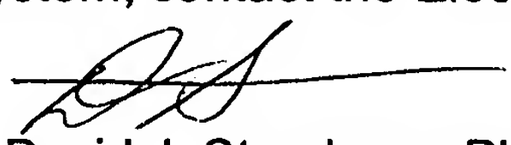
Claims 35-38 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Thursday, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1656